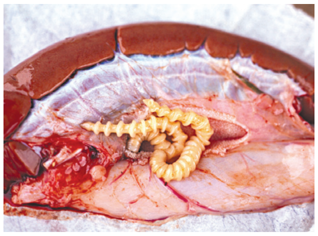

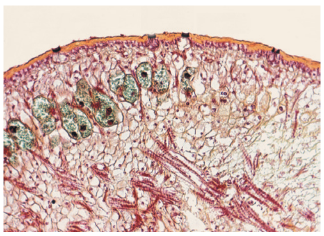

16

Pentastomiasis

Wayne M. Meyers and Ronald C. Neafie

Introduction

Definition

Pentastomiasis is infection by pentastomes, which are organisms in the phylum Pentastomida (the approximately 95 species of the phylum, most correctly called pentastomids, are commonly known as pentastomes and will be so termed in this chapter). The single class within the phylum, Pentastomata, comprises 7 families in 2 orders, Porocephalida and Cephalobaenida. In the order Cephalobaenida, infections in humans by *Raillietiella hemidactyli* and *Raillietiella gehyrae* have been reported. Two families of the order Porocephalida—Porocephalidae and Linguatulidae—afflict humans. Infections by *Armillifer moniliformis, Armillifer grandis, Armillifer agkistrodontis, Armillifer najae, Leiperia cincinnalis*, and *Sebekia* sp are known[1,2] however, 2 species of porocephalida, *Armillifer armillatus* and *Linguatula serrata*, account for nearly all infections in humans.

Synonyms

Pentastomiasis is also known as porocephaliasis. Infection by *L. serrata* is sometimes called linguatuliasis, but is more commonly known as tongue worm infection. Colloquial names for pentastomiasis include golf caddy's disease (Democratic Republic of the Congo (DRC)), halzoun (Middle East), and marrara (Sudan, Southwest Asia).

General Considerations

Adult pentastomes are bloodsucking endoparasites of terrestrial vertebrates, almost exclusively reptiles, birds, and mammals (Figs 16.1 to 16.3). The name pentastome derives from an ancient misidentification of the 4 hooks and 1 mouth on the anterior end of the organism as 5 mouths.

The phylogeny of pentastomes has long been a puzzle. Various interpretations of the natural history of the Pen-

Figure 16.1
Rock python, a common definitive host of *Armillifer armillatus* in Africa.

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Figure 16.2
Autopsy of rock python in Bas-Congo, DRC. Lung, digestive tract, and liver are being removed.

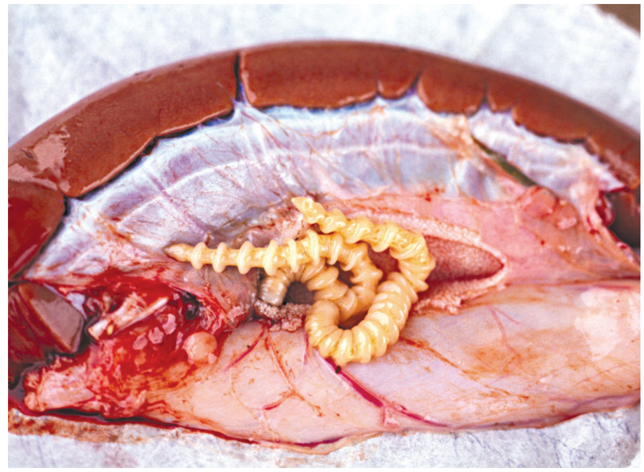

Figure 16.3
Two adult *Armillifer armillatus* attached to respiratory epithelium of rock python shown in Figure 16.2. Lung has been incised to reveal adult pentastomes.

Figure 16.4
Adult female of *Armillifer armillatus* (10 by 0.8 cm) attached to respiratory epithelium of rock python shown in Figures 16.2 and 16.4. Note short cephalothorax (arrow) and long annulated abdomen.

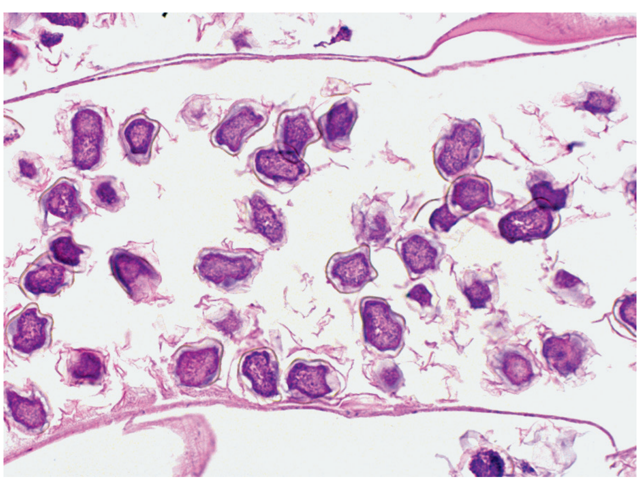

Figure 16.5
Eggs in section of oviduct of adult pentastomes in snake lung. X120

tastomida place their possible divergence during the Cambrian explosion of multicellular organisms. Taxonomists initially placed them in either the phylum Annelida or the phylum Arthropoda.[3] Recent evidence, including molecular biologic findings, strongly suggests that pentastomes are closely related to crustacean arthropods, but most authorities today retain the unique minor phylum Pentastomida for these organisms.[4,5,6] A more comprehensive phylum called Lobopodia, which would include the closest relatives of the Arthropoda, such as pentastomes and related fossil forms, is under consideration.[7,8,9]

Pentastomiasis was among the earliest zoonotic parasitic diseases to be described. Pruner first described the infection in humans in Egypt in 1847. A year later, in Africa, Wyman discovered adult pentastomes in pythons.

Epidemiology

Pentastomiasis is widespread, with most infections in humans occurring in Asia and tropical Africa. In Africa, infection is commonly by *A. armillatus*. In Asia, North Africa, Europe, and the Western Hemisphere, *L. serrata* is usually the infecting species, although rare imported *A. armillatus* infections have been reported.[10,11] *Porocephalus taiwana* infects humans in China.[2,12,13] Estimates of minimal prevalences have been established by detection of calcified, C-shaped, encysted larvae in radiologic films of the abdomen.[14] This method revealed a prevalence of 40% in midwestern Nigeria.[15] Autopsy series probably produce more accurate data. In Malaysia, larval pentastomes were found in over 45% of a series of consecutive autopsies from an aboriginal population.[16] A study in the DRC found an autopsy prevalence of 23%.[17] Seroepidemiologic surveys have so far yielded prevalences lower than those derived from autopsy.[18] However, advances in the serologic detection of pentastomiasis may provide more accurate data.[19,20]

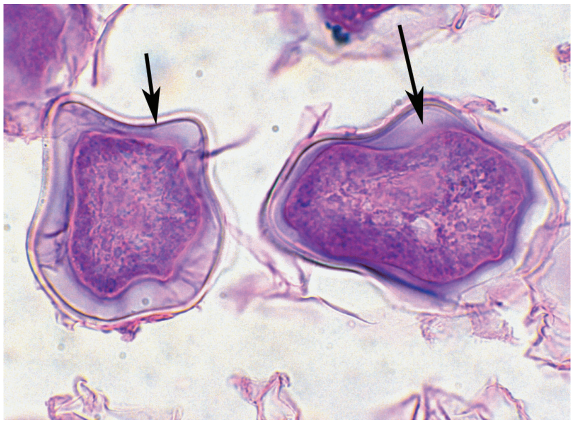

Figure 16.6
Higher magnification of unembryonated eggs in Figure 5, demonstrating thin outer shell (short arrow) and thick inner shell (long arrow). X600

Figure 16.7
Third-stage infective (nonencysted) larva of *Armillifer armillatus* attached to peritoneal surface of diaphragm, found at autopsy in Congolese patient. X3

Infectious Agent

Morphologic Description

Adult pentastomes are elongate and cylindrical or flat. In many species, the body is divided into 2 distinct regions: a short cephalothorax and a long abdomen (Fig 16.4). The cephalothorax is crowned by a mouth and 2 pairs of chitinized hooks. In some species (especially *A. armillatus*), pseudoannulations encircle the abdomen, but the body is not segmented. The number of annuli is a useful identifying feature—for example, 18 to 22 annuli in *A. armillatus*; 30 in *A. moniliformis*. Adults are a few millimeters to 15 cm long, depending on the species, and males are generally much smaller than females. Pentastomes have an extensive reproductive system and a primitive digestive tract, but no circulatory or respiratory system. Paired frontal glands lie alongside the gut for much of its length. Ducts from these glands open to the cuticular surface on the cephalothorax.[20,21] In the female, the genital pore is located on either the anterior (Cephalobaenida) or posterior (Porocephalida) end.

Pentastome eggs are ovoid and double-shelled (Figs 16.5 and 16.6). Eggs vary considerably in size according to species (average 105 by 125µm) and are embryonated when deposited. The embryo emerges as a first-stage larva with rudimentary appendages (see life cycle). The larva molts twice, loses its appendages, and develops into a third-stage larva, the infective form commonly found in humans (Fig 16.7). The larva attaches to host tissue by hooks on its anterior end (Fig 16.8). Although smaller, infective third-stage larvae are morphologically similar to adult pentastomes. The cuticle of the third-stage larva is smooth (Fig 16.9) in all species infecting humans except *L. serrata*, which has a spiny cuticle (Figs 16.10 and 16.11).

In tissue sections, larvae display several distinctive histologic anatomic features.[22] In cross section, the frontal glands, also called acidophilic glands, appear as red aggregates of cells and matrix around the digestive tube (Fig 16.12). The cuticle is 5 to 10 µm thick and has sclerotized openings (Figs 16.9 and 16.13). The subcuticular area contains subcutaneous glands, and striated muscle fibers are arranged in circular and longitudinal patterns in the organism's parenchyma (Fig 16.9).[23]

Life Cycle and Transmission

Each stage in the life cycle of a pentastome is parasitic. Adult Porocephalidae inhabit the respiratory passages of reptiles, and adult Linguatulidae the nasal passages of mammals. Numerous species of vertebrates serve as intermediate hosts, including humans, nonhuman primates,dogs and, most commonly, rodents.[13,24-26] Direct infection that bypassed the intermediate host has been seen in stressed captive lizards, but in such instances the infective larvae did not develop into adults.[27] Occasionally, both adults and third-stage larvae have been found in infected snakes, representing true autoinfection.[28]

The life cycle of *A. armillatus* typifies the stages of a common porocephalida pentastome in the definitive (snake) and intermediate (usually rodent) host (Fig 16.14). Using their anterior hooks, male and female adults attach to the respiratory epithelium of snakes such as the rock python (*Python sebae*) and some cobras and vipers (Fig 16.3). Copulation takes place 3 to 4 months after infection of a definitive host. Approximately 4 to 8 months later, fertilized females begin to deposit embryonated eggs. The eggs are carried by respiratory secretions to the snake's oral cavity, where they are either discharged or swallowed and ejected in the feces.[29,30] Vegetation and water contaminated with these eggs are sources of infection for intermediate rodent hosts.

In rodents, ingested eggs hatch, releasing first-stage larvae in the digestive tract. Larvae apparently use a stylet ex-

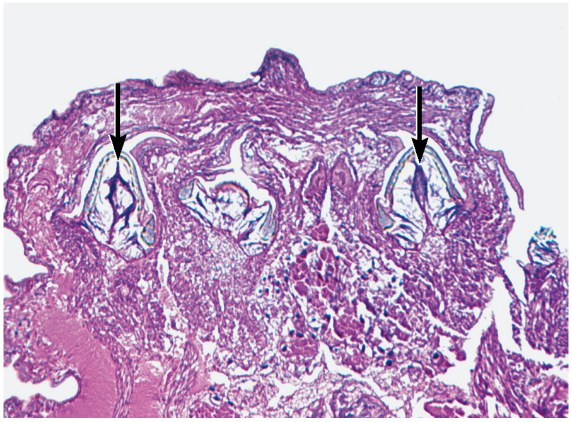

Figure 16.8
Section of anterior end of pentastome larva removed from human gut wall, showing 2 of 4 hooks (arrows). X57

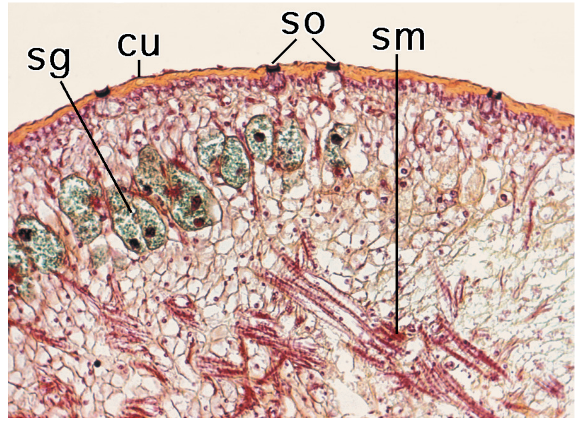

Figure 16.9
Section of *Armillifer armillatus* removed from human liver. Cuticle (cu) is smooth but punctuated by sclerotized openings (so). Subcuticular glands (sg) and striated muscle (sm) are prominent. Movat X60

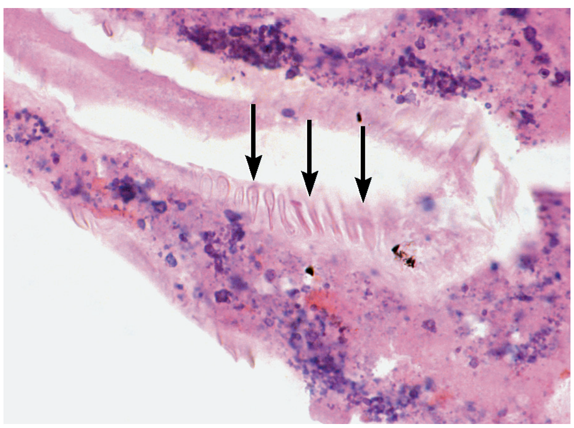

Figure 16.10
Cuticle of degenerated *Linguatula serrata* in liver, showing numerous spines (arrows). X380

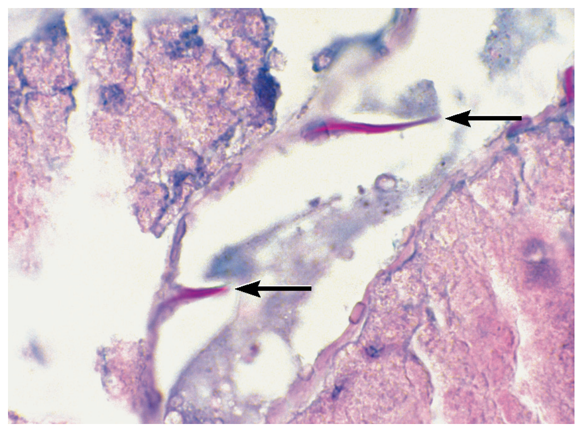

Figure 16.11
Spines (arrows) on degenerated cuticle of *Linguatula serrata* are acid-fast with Ziehl-Neelsen stain. X600

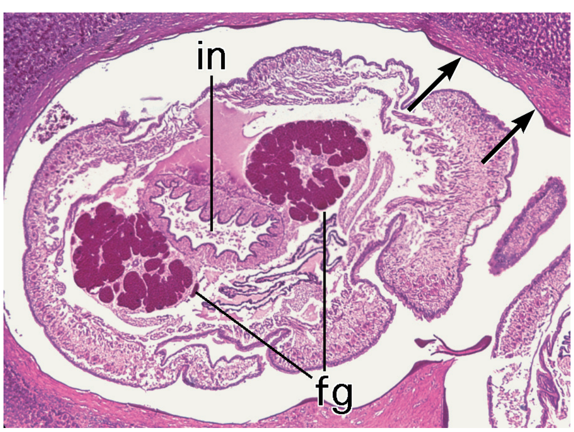

Figure 16.12
Encysted *Armillifer armillatus* larva in liver. Shed cuticle from previous molt lines cyst wall (arrows). Acidophilic frontal glands (fg) lie along intestine (in). X21

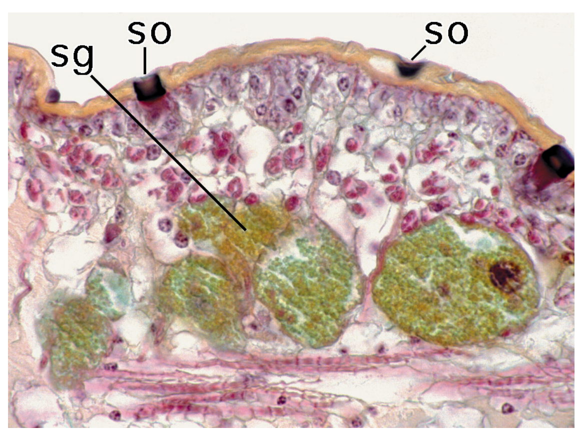

Figure 16.13
Detail of encysted infective larva in lung. Black cylindrical sclerotized openings (so) in cuticle and green subclavicular glands (sg) are prominent in Movat-stained section. X425

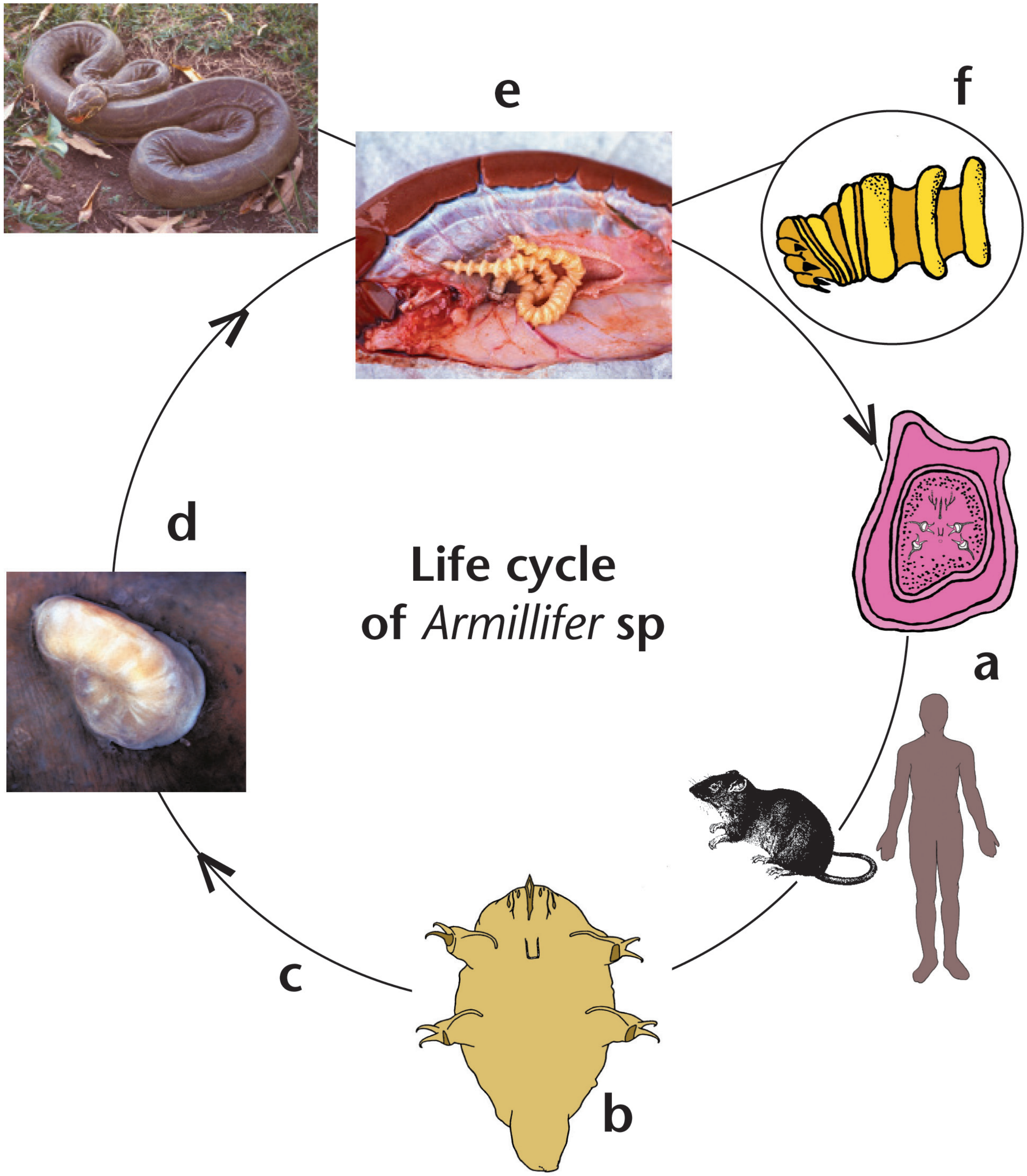

Figure 16.14
Life cycle of *Armillifer* sp. **a**) Eggs (usually embryonate and passed in respiratory secretions, saliva, or feces are ingested by secondary host—usually a rodent. **b**) 1st stage larva emerge, penetrate gut of secondary host, migrate, and encyst in various host tissues. In humans, invasion by 1st-stage larvae is asymptomatic. **c**) Larvae molt twice. **d)** 3rd-stage larvae in tissues of animal or human secondary host can excyst and migrate. In natural infection, encysted and free larvae ingested by definitive host migrate to respiratory tract to complete development. Photo shows encysted larva. e**)** Adults inhabit respiratory tract of definitive host (African rock python shown). **f**) Head of adult *Armillifer* sp has 4 hooks for attaching to host tissue.

Figure 16.15
Encysted *Armillifer armillatus* larva on liver of Congolese adult. Cyst is 0.6 by 1 cm and characteristically C-shaped.

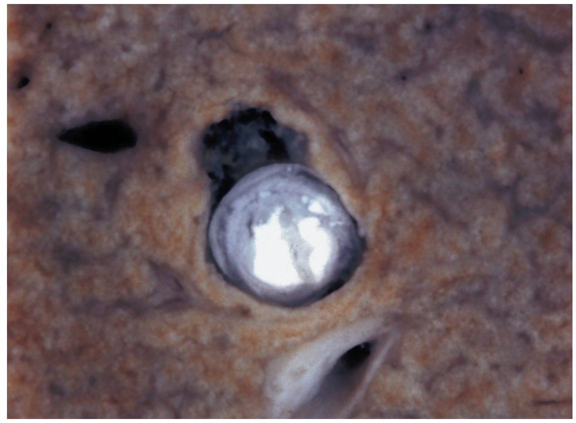

Figure 16.16
Cut surface of liver from patient described in Figure 16.15, showing encysted *Armillifer armillatus*. Cyst is 3 mm in diameter.

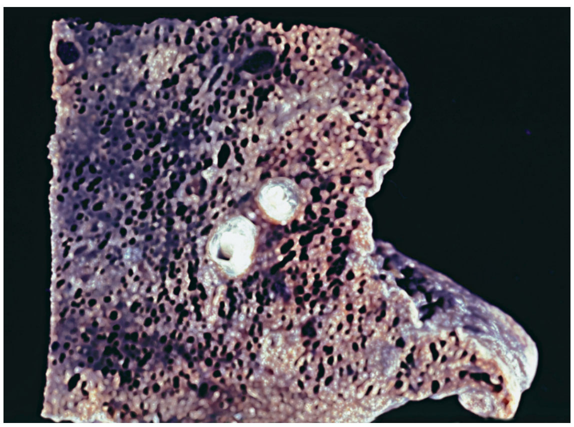

Figure 16.17
Two encysted *Armillifer armillatus* larvae in cut surface of lung of patient described in Figure 16.15. Larvae are 3 mm in diameter.

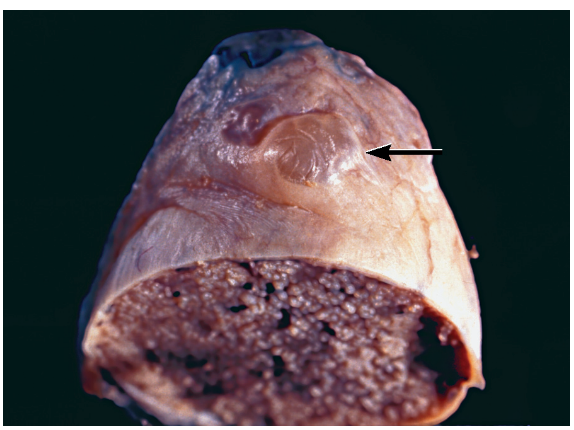

Figure 16.18
Encysted *Armillifer armillatus* larva (arrow) in tunica of testis of patient described in Figure 16.15. Cyst is 1.5 by 1 cm.

tending from their anterior end to penetrate the rodent's gut wall, although enzymatic activity of the frontal gland secretions may play a role in tissue invasion.[20] From observations on a pentastome of alligators (*Sebekia mississippiensis*), Boyce and Kazacos showed that larval pentastomes could breech the gut wall of experimentally infected hamsters, a potential paratenic host for this parasite, in 1 to 3 days.[31] First-stage larvae may migrate by passing through the entire thickness of the gut wall and entering the abdominal cavity, or by invading a blood or lymphatic vessel in the gut wall, mesentery, omentum, or other intra-abdominal site, and spreading hematogenously.[23] By whichever route, larvae can disseminate rapidly and widely in an intermediate host. At this stage, larvae lose their appendages, molt, and encyst in or on virtually any organ or structure (Figs 16.15 to 16.18). Whether or not all larvae encyst is controversial. A series of several molts results in infective third-stage larvae, often called nymphs. The cycle is maintained when a definitive snake host devours an infected intermediate host, usually a rodent. In the snake, infective larvae migrate from the stomach up the esophagus and into the lung, where they mature into adults and complete the life cycle. In aberrant intermediate hosts (humans or other large mammals), larvae eventually die, interrupting the life cycle.

The life cycles of all the pentastomes that infect humans vary in ways too numerous to describe here, but the life cycle of *L. serrata* deserves brief mention. Adult *L. serrata* inhabit the nasopharynx of mammalian carnivores such as dogs, foxes, or wolves. Embryonated eggs exit in nasal secretions of these definitive hosts. Herbivorous animals (intermediate hosts, typically sheep and goats) ingest the embryonated eggs. Eggs hatch, releasing first-stage larvae that penetrate the gut and develop and encyst in a manner similar to *A. armillatus*. When humans ingest first-stage *L. serrata* larvae, the larvae likewise penetrate the gut and encyst in various tissues (Fig 16.19). The normal life cycle is completed when a carnivorous definitive host devours the

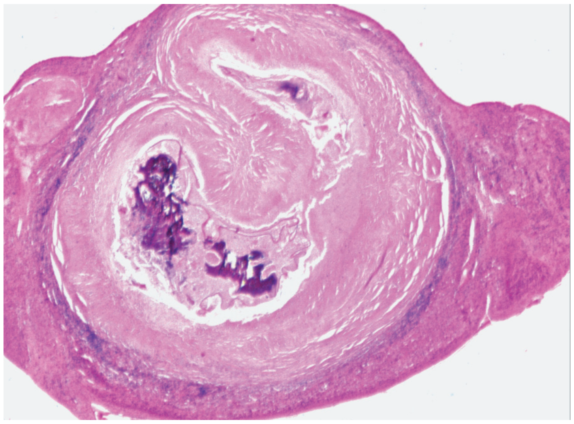

Figure 16.19
Section of degenerating *Linguatula serrata* larva in human liver. Note mineralization, which appears in radiographs as C-shaped opacity. X15

Figure 16.20
Larva of *Armillifer armillatus* extracted from inflammatory mass in conjunctiva of adult Congolese.

flesh of an intermediate host. When humans eat improperly cooked or raw flesh of an intermediate host, infective larvae migrate to the throat, where they attach and provoke the halzoun or marrara syndromes. Larvae of *L. serrata* have rarely developed into adults in the nasal cavity of humans.

Clinical Features and Pathogenesis

Humans are usually highly tolerant of infection by pentastomes. Some authorities attribute this tolerance to the immunomodulatory effect of the frontal gland secretions that coat the larvae's cuticle and facilitate evasion of the host immune response.[20] The initial phase of pentastomiasis in all intermediate hosts is probably the penetration of the gut wall by first-stage larvae, after embryonated eggs have been ingested in contaminated meat, water, or vegetation. This asymptomatic phase has been described in animals but never directly observed in human tissue. In the abdomen, first-stage larvae molt twice and develop into infective third-stage larvae. Most, but not all, third-stage larvae encyst and lodge in various sites, showing a predilection for the mesentery and peritoneum, and on or within parenchymatous abdominal organs. First-stage larvae that enter the lymphatic or blood system in the gut wall frequently invade the lungs and occasionally the brain, but may appear in virtually any site.

Even when infection involves numerous third-stage larvae, pentastomiasis is usually asymptomatic. However, as the developing larvae gradually enlarge, they may exert pressure on surrounding structures, causing complications such as biliary obstruction. In the eye, pentastomes may cause multiple lesions, including iritis, subluxation of the lens, secondary glaucoma, conjunctivitis, and invasion of lacrimal caruncles.[32,33,34] Figures 16.20 to 16.23 depict a larva of *A. armillatus* extracted from a conjunctival mass near the lacrimal caruncle of a Congolese patient. When excised, the mass, which had developed over the course

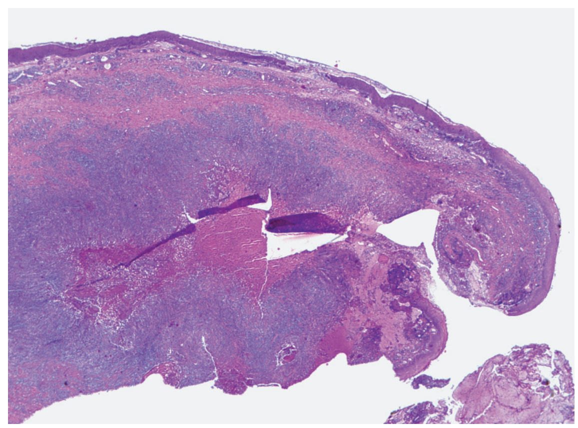

Figure 16.21
Section of inflammatory mass in conjunctiva of patient described in Figure 16.20. X110

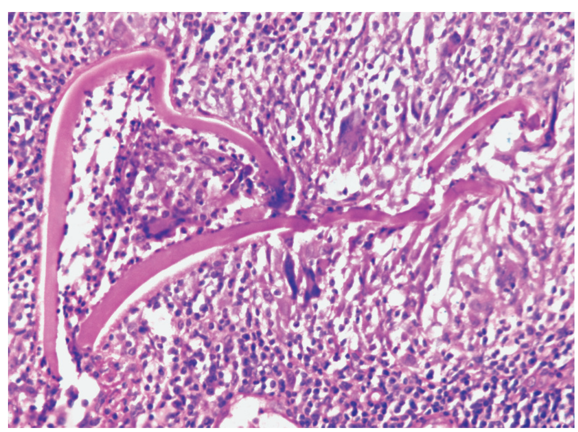

Figure 16.22
Detail of Figure 21 showing cuticular fragments from earlier molt of pentastome larva depicted in Figure 20. X 175

Figure 16.23
Movat pentachrome stain reveals black cylindrical sclerotized openings (arrows) in cuticular fragment shown in Figure 16.22. X430

Figure 16.24
Encysted *Armillifer armillatus* larva in human lung demonstrating typically slight tissue reaction in intermediate host. Movat x11

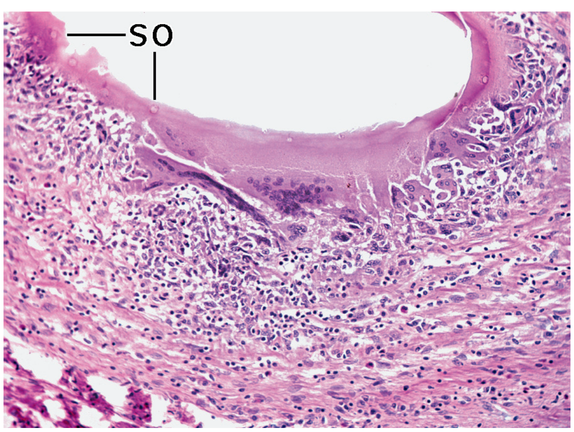

Figure 16.25
Degenerating cyst of *Armillifer armillatus* larva in intra-abdominal lymph node. Sclerotized openings (so) confirm diagnosis of pentastomiasis. X100

of a year and caused marked chronic irritation, had areas of extensive inflammation in which there were identifiable cuticular elements of a pentastome, such as the diagnostic sclerotized openings. Although numerous other conditions have been attributed to pentastomes, including pneumonitis, collapsed lung, peritonitis, nephritis, meningitis, and pericarditis, in most cases only a tenuous causal relationship has been established.[35,36,37]

Patients sometimes present with acute abdominal symptoms, and intestinal obstruction has been observed. Most often, however, laparotomy findings reveal only variable numbers of encysted larvae[38] or nonencysted free or attached larvae. Intestinal adhesions are sometimes associated with pentastomiasis.[39] Pentastomiasis may mimmic hepatoma clinically.[40] Pentastomiasis has resulted in 2 reported fatalities. One patient died of fulminant septicemia.[36] The other, a 5-year-old girl, had a massive *A. grandis* infection that produced generalized disease, with large numbers of larvae in the lung and brain. It was suggested that the patient had ingested a gravid pentastome.[5,41] In 1989, Mairena et al described a dermatitis caused by a *Sebekia* sp larva in Costa Rica.[42] The patient presented with marked peripheral eosinophilia and a pruritic serpiginous burrow on the abdomen, from which a 1 cm long larva was removed. Some researchers speculate that pentastomes provoke malignancies.[43] Based on our own observations and those of Fain[44] and Hopps et al,[28] we consider the association of pentastomiasis and cancer to be tenuous.

The halzoun and marrara syndromes are characterized by discomfort in the nasopharynx and throat, accompanied by paroxysmal coughing, sneezing, and sometimes dysphagia and vomiting.[45] These syndromes result when third-stage larvae ingested in raw flesh of an intermediate host migrate from the upper gastrointestinal tract to the throat and nasopharynx. Halzoun and marrara are most common in the Middle East and the Sudan. Hypersensitivity reactions may lead to dyspnea or even fatal asphyxia. Rarely, infective larvae in the nasopharynx develop into adults.

Pathologic Features

In a definitive host, adult pentastomes do not provoke significant tissue reaction (Figs 16.3 and 16.4).[28] Flach et al depict a primary larva of a *Sambonia* sp pentastome in the intestinal wall of a monitor lizard (*Varanus exanthematicus*) provoking only slight cellular response.[27] In an intermediate host, tissue reaction to pentastome larvae varies[31] but is usually slight (Fig 16.24), suggesting to some authorities that the excretory/secretory proteins coating the cuticle of pentastomes may have immunomodulatory properties.[20,46] Inflammatory response around larvae can nevertheless be marked (Fig 16.21). In animals, the route of invasion has been described. In humans, although it has not been observed, the gastrointestinal tract is the presumed route of

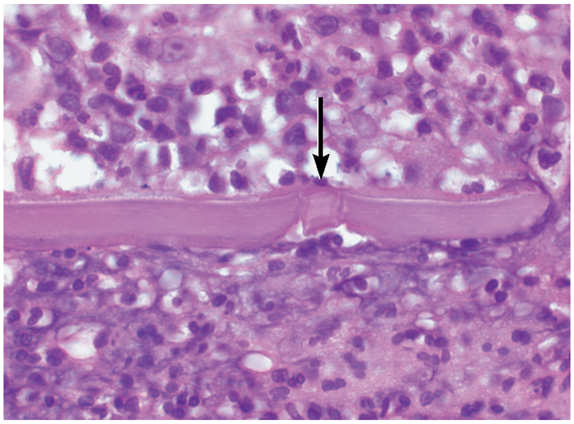

Figure 16.26
Conjunctival lesion containing fragment of cuticle of *Armillifer armillatus* larva. Sclerotized opening (arrow) is readily seen in H&E-stained section. X590

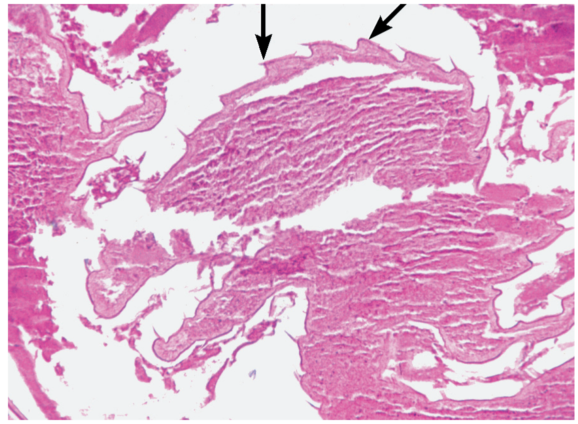

Figure 16.27
Cuticular fragments of *Linguatula serrata* with numerous cuticular spines (arrows). X135

invasion. Within the intestinal wall, or soon after breeching it, larvae develop into advanced forms within the abdominal cavity, or enter lymphatic or blood vessels and disseminate.[5,12,47] Following a series of molts, third-stage larvae usually encyst on or within abdominal organs or the peritoneum.[48] We have observed numerous infective larvae of *A. armillatus* at autopsies in the DRC. In the abdominal cavity of a single cadaver, we have observed encysted, nonencysted-free, and nonencysted-attached infective larvae (Figs 16.7, and 16.15 to 16.18). It is possible that the free forms had excysted after the death of the host, but since no sites consistent with recently evacuated cysts were identified, it is more likely that the free forms had never encysted.

Typically, a cyst encases a larva in a thin fibrous wall (Figs 16.12 and 16.24). As the larva molts, cuticular material merges with the lining of the cyst wall, preserving in these layers the pentastome's sclerotized cuticular openings (Fig 16.25). The same process preserves the spines of an *L. serrata* larva. After a few years, the encysted larva dies, and a granuloma may develop in response to the antigenic products of degeneration.[49] A degenerating larva can be identified by the sclerotized openings in cuticular elements—usually the longest-lasting remnants. A hyalinized calcified nodule is the final stage of an encysted pentastome (Fig 16.19).

Diagnosis

Calcified encysted third-stage larvae are usually an incidental finding in radiographs of the abdomen or at surgery or autopsy. Histopathologic diagnosis can usually be readily made by demonstrating typical morphologic features in well-preserved larvae. Even in highly degenerated larvae, the unique sclerotized openings in the cuticle are often detectable in H&E-stained sections (Fig 16.26); however, the Movat pentachrome stain demonstrates these structures best (Fig 16.13). Cuticular spines, that may be acid-fast, distinguish *L. serrata* larvae from *A. armillatus* larvae (Figs 16.10, 16.11, and 16.27). Serologic tests using immunofluorescence, gel diffusion, and immunoelectrophoresis are available but not highly sensitive.[18] An ELISA based on the 48 kDa frontal gland metalloproteinase of pentastomes may increase the efficacy of serologic testing.[19] Molecular methods are available for some species.[13]

In tissue sections, pentastomes can be mistaken for any parasitic metazoan, especially cysticerci, spargana, nematodes, and fly larvae. However, none of these organisms has sclerotized openings in the cuticle, and cysticerci, spargana, and nematodes do not have striated muscle. Fly larvae do have striated muscle, but they also have numerous tracheal tracts which pentastomes do not have.

Treatment and Prevention

Pentastomiasis in humans does not usually require treatment. However, patients who become symptomatic, such as those with halzoun or marrara, may require surgical removal of free or encysted parasites in the eye, throat, or nasal passages. Hypersensitivity reactions brought on by these syndromes may be treated with antihistamines and/or corticosteroids. Exploratory surgery may be warranted for patients with acute abdominal symptoms or those with radiologic or serologic evidence of pentastomiasis. Infected mammals, snakes, and captive monitor lizards have been successfully treated with ivermectin, sometimes combined with corticosteroids to reduce inflammation and surgery to remove dead pentastomes.[27,50] There are no reports of humans being treated with ivermectin, but the drug's efficacy in humans should be investigated. Diethylcarbamizine has been suggested as a treatment for linguatuliasis, but its usefulness has not been established.

In general, pentastome infections in humans can be pre-

vented by adequate sanitary precautions and by avoiding the consumption of raw snake and other exotic meats.

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